

We Claim:

1. A method for selecting a dimerizing test polypeptide, comprising:
  - i providing a population of host cells wherein each host cell contains
    - (a) a chimeric gene which encodes a fusion protein, including one or more DNA-binding domains, an activation domain, and a test polypeptide,
    - (b) a reporter gene operably linked to a transcriptional regulatory sequence which includes two or more binding sites (DBD recognition elements) for the DNA-binding domain of (a),wherein binding of a single copy of the fusion protein to the transcriptional regulatory sequence of the reporter gene does not result in a desired level of expression of the reporter gene;  
wherein dimerization and binding of the fusion protein to the transcriptional regulatory sequence of the reporter gene results in a desired level of expression of the reporter gene;
  - ii isolating host cells exhibiting a desired level of expression of the reporter gene thereby selecting a dimerizing test polypeptide.
2. The method of claim 1, wherein the host cell further comprises a second reporter gene operably linked to a transcriptional regulatory sequence comprising one binding site for the DNA binding domain of (a).
3. The method of claim 1, further comprising isolating a polynucleotide comprising a sequence encoding the dimerizing test polypeptide.
4. The method of claim 3, further comprising linking the sequence encoding the dimerizing test polypeptide to a heterologous sequence.
5. The method of claim 1, wherein the host cell is a prokaryotic host cell.

6. The method claim 1, wherein the desired level of expression of the reporter gene confers a growth advantage on the host cell.
7. The method of claim 1, wherein the desired level of expression of the reporter gene produces a detectable signal.
8. The method of claim 1, wherein the chimeric gene is a member of a library comprising a plurality of sequences encoding for random test polypeptides.
9. The method of claim 8, wherein the library comprises at least  $10^7$  members.
10. A method for selecting a composite transcription factor, comprising:
- i providing a population of host cells wherein each host cell contains
    - (a) a chimeric gene which encodes a fusion protein, including one or more DNA-binding domains, an activation domain, and a test polypeptide,
    - (b) a gene which encodes for a DNA-binding domain of known specificity,
    - (c) a reporter gene operably linked to a transcriptional regulatory sequence which includes at least one binding site (DBD recognition elements) for the DNA-binding domain of (a) and at least one binding site for the DNA-binding domain of (b),

wherein binding of either of the DNA-binding domain of (a) or (b) to the transcriptional regulatory sequence of the reporter gene does not result in a desired level of expression of the reporter gene;

wherein formation of a dimer between (a) and (b) and binding of the dimer to the transcriptional regulatory sequence of the reporter gene results in a desired level of expression of the reporter gene; and
  - ii isolating host cells exhibiting a desired level of expression of the reporter gene thereby selecting a composite transcription factor.

11. The method of claim 10, wherein the host cell further comprises a second reporter gene operably linked to a transcriptional regulatory sequencing comprising one binding site for the DNA binding domain of (a).

12. The method of claim 10, wherein the host cell is a prokaryotic host cell.

13. The method claim 10, wherein the desired level of expression of the reporter gene confers a growth advantage on the host cell.

14. The method of claim 10, wherein the desired level of expression of the reporter gene produces a detectable signal.

15. The method of claim 10, wherein the chimeric gene is a member of a library comprising a plurality of sequences encoding for random test polypeptides.

16. A method for detecting an interaction between a test polypeptide and a DNA sequence, comprising:

- i providing a population of host cells wherein each cell contains
  - (a) a first reporter gene operably linked to a transcriptional regulatory sequence which includes one or more binding sites (DBD recognition elements) for a DNA-binding domain,
  - (b) a second reporter gene operably linked to a transcriptional regulatory sequence which includes one or more binding sites (DBD recognition elements) for a DNA-binding domain,
  - (c) a chimeric gene which encodes a fusion protein, the fusion protein including a test polypeptide, a weak DNA-binding domain and an activation tag,

wherein binding of the weak DNA-binding domain of (c) to the binding sites of (a) or (b) does not cause a significant increase in the expression of the first reporter gene or the second reporter gene;

wherein expression of the first reporter gene results in a first detectable signal;

wherein expression of the second reporter gene results in a second detectable signal;

wherein a non-specific interaction between a test polypeptide of the fusion protein and a DBD recognition element of the first and second reporter genes results in an increased level of expression of the first and second reporter genes;

wherein a specific interaction between a test polypeptide of the fusion protein and a DBD recognition element of the first or second reporter gene results in a desired level of expression of either the first or second reporter gene; and

ii isolating host cells comprising a fusion protein that specifically interacts with a DBD recognition element of the first or second reporter gene exhibiting a desired level of expression of the first or second reporter gene, thereby detecting an interaction between the test polypeptide and a DBD recognition element DNA sequence.

17. The method of claim 16, wherein the chimeric gene is a member of a library comprising a plurality of sequences encoding for random test polypeptides or the DNA-binding domain recognition element of one of the reporter genes is a member of a library.

18. The method of claim 16, wherein the weak DNA-binding domain comprises two Cys<sub>2</sub>His<sub>2</sub> zinc fingers.

19. The method of claim 16, further comprising isolating a polynucleotide comprising a sequence encoding the test polypeptide.

20. The method of claim 19, further comprising linking the sequence encoding the test polypeptide to a heterologous sequence.